PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Effects of cancer treatment on household impoverishment: a multicenter cross-sectional study in China
AUTHORS	Fu, Wenqi; Shi, Jufang; zhang, xin; Liu, Chengcheng; Sun, Chengyao; Du, Yupeng; Wang, Hong; Liu, Chaojie; Lan, Li; Zhao, Min; Yang, Li; Bao, Burenbatu; Cao, Sumei; Zhang, Yongzhen; Wang, DeBin; Li, Ni; Chen, Wanqing; Dai, Min; Liu, Guoxiang; He, Jie

VERSION 1 – REVIEW

REVIEWER	Anli Leng Shandong University, China
REVIEW RETURNED	14-Nov-2020

GENERAL COMMENTS	This paper examines the incidence and intensity of household impoverishment induced by cancer treatment in China. It's very meaningful. However,I have some questions. 1)More than 85% of cancer patients came from the central (developing) and western (under-developed) regions. There are only 15% of cancer patients came from the eastern (developed) regions. However, the eastern region is densely populated actually in China.More than half the population lives in the east. I'm worried about the representativeness of the sample. I am also worried the incidence and intensity of household impoverishment induced by cancer treatment in this paper are higher than those of the actual national average. 2)How many patients are diagnosed with cancer in stage III or stage IV? In general, the most of the treatment costs occur in the advanced stages of cancer, which is more likely to push patients into poverty.

REVIEWER	Ciaran O'Neill Queen's University Belfast Faculty of Medicine Health and Life Sciences, Centre for Public Health
REVIEW RETURNED	08-Dec-2020

GENERAL COMMENTS	This is an interesting paper making a potentially valuable contribution to the literature. It could usefully be clarified in a number of areas. First, the administration of the survey and its content remain somewhat unclear to me - patients with a diagnosis of cancer

	other than metastatic cancer(?) were identified from hospital records and then approached for survey? The survey covered expenditures but it is not entirely clear what was and what was not covered in this - use of an online supplement may assist here. Second, the apparent exclusion of important items such as non-medical costs related to travel is acknowledged as a limitation as is the exclusion on information on how expenditures are covered - e.g. recourse to borrowing - though sale of assets could usefully have been added here. But I remain somewhat unclear as to how distance from the poverty line was calculated. Third, I am unclear as to how national estimates of impovrishment were produced - was the sample weighted somehow? Fourth, access to care will be an important determinant of impovrishment. Care may not have been consumed because it could not be afforded, while this is alluded to it is an issue that is not adequately discussed in the paper Some more detail on the regression analysis could usefully be provided - I think they used forward selection in choice of independent variables - but they do not discuss goodness of fit.

REVIEWER	Peter Rohloff Wuqu' Kawoq | Maya Health Alliance- Guatemala
REVIEW RETURNED	13-Dec-2020

GENERAL COMMENTS	This is a very interesting paper on an important topic. I mostly have minor clarifying questions: Introduction: - In the introduction or discussion, I think more detail about what the different insurance schemes offer and who they serve would be helpful to help better interpret the results. Also, some discussion of what is publicly paid for in cancer treatment and what patients are typically expected to pay OOP – do we know for example if there are legitimate unpaid costs of treatment or are their illegal or under-the-table user fees? Methods: - Can you justify the time line (for why the eligibility window was chosen). - Can you clarify what is meant by exclusion of those with “cancer in multiple organs”? Is this metastatic cancer or two separate primary cancers? If the former, then this is a weakness of the paper and we need some detail about the proportion of cancer that is metastatic and the reasons that it was excluded from analysis. Especially in rural underserved areas I would expect a lot of cancer would be metastatic at diagnosis and represent a very significant portion of the total burden. - In the abstract, and methods, the statement about assuming that individuals would divert discretionary spending to cancer treatment, and about treating diagnostic OOP costs as part of pre-treatment consumption – I am unclear on what this means. From reading the methods it seems like OOP costs for cancer treatment were estimated and all household consumption costs were also estimated. I assume the poverty line estimates were based on all household consumption minus whatever was spent on cancer

	treatment, so I am unclear what those other statements are meant to indicate - Some more detail on how the cost ascertainment tools were developed might be helpful (perhaps an appendix with the tool). Was household income just asked and, if so, how? Or was income estimated from consumption indicators? Are there standard approaches to household consumption measures in the authors' region that were used? Results: - As the authors note a weakness here is the use of recall data. One possible sensitivity analysis would be to examine for systematic differences in estimates if caregivers vs patients provided these estimates – this would be one way to look at one form of recall variability/bias. - Throughout the results section, I wonder about the interaction between the rural/urban and region (eastern/central/western) variable. Particularly that region is significant but urban/rural not in the adjusted regression. I assume region is captured a significant component of "rurality" but can the authors explain this a bit more? - -Table 1 could be simplified by eliminating the X2 statistics and leaving the P values and a footnote that these are X2 tests. - For insurance status, does "Others" mean "no insurance" or "private insurance" or both? It seems like this is an important point – explicitly comparing impoverishment by social security vs no insurance status. - Seems like a Table that summarizes the key findings of the consumption/income audit would be very helpful. What is the per capita consumption pre and post? How about income? Does income fall post treatment (people losing their jobs)? What are the major categories of consumption and which are most impacted by cancer treatment spending? Where are households deciding to cut costs? - Similarly are the details of OOP spending (total amounts and categories) available? Where are the insurance programs failing? What categories of things are people needing to spending money on – for example is it food and lodging or is it payments for stocked out medicines that the public sector should be providing? Where the deficits are says a lot about where improvements could be made or where the problems lie.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: AnliLeng
Institution and Country: Shandong University, China
1) More than 85% of cancer patients came from the central (developing) and western (under-developed) regions. There are only 15% of cancer patients came from the eastern (developed) regions. However, the eastern region is densely populated actually in China. More than half the population lives in the east. I'm worried about the representativeness of the sample. I am also worried the incidence and intensity of household impoverishment induced by cancer treatment in this paper are higher than those of the actual national average.
Response: Thanks for making this important point. We agree that the sample was biased. The stratified sampling strategy ensured that the minimal sample size could be met in all of the three regions. However, the eastern region was under-represented. In the revised manuscript, we applied a weighting system based on the number of new cancer cases: 0.48 for eastern, 0.28 for central, and

0.24 for western. Indeed, the weighted estimation resulted in a lower national average in incidence and intensity of household impoverishment compared with the non-weighted ones. We discussed the sampling bias as part of the limitations of the study (paragraph 4 on page 5 & paragraph 3 on page 15).

2) How many patients are diagnosed with cancer in stage III or stage IV? In general, the most of the treatment costs occur in the advanced stages of cancer, which is more likely to push patients into poverty.
Response: Thanks for the advice. We have added relevant data in the manuscript: 15.86% in stage III and 11.64% in stage IV. However, the stages of cancer were not found to be associated with household impoverishment (paragraph 5 on page 4).

Reviewer: 2
Reviewer Name: Ciaran O'Neill
Institution and Country: Queen's University Belfast Faculty of Medicine Health and Life Sciences, Centre for Public Health
First, the administration of the survey and its content remain somewhat unclear to me - patients with a diagnosis of cancer other than metastatic cancer (?) were identified from hospital records and then approached for survey?
Response: Sorry for the lack of clarity. Eligible participants were those who had one primary cancer (including metastatic cancer). Those with two or more primary cancer diagnoses were excluded. The eligibility of study participants was assessed through the hospital records (paragraph 5 on page 4).
The survey covered expenditures but it is not entirely clear what was and what was not covered in this - use of an online supplement may assist here.
Response: Thanks for the constructive suggestion. We have attached a supplementary file (Table S2) to list the expenditure items.
Second, the apparent exclusion of important items such as non-medical costs related to travel is acknowledged as a limitation as is the exclusion on information on how expenditures are covered - e.g. recourse to borrowing - though sale of assets could usefully have been added here.
Response: We agree. In addition to the exclusion of non-medical costs, the missing information on how the expenses were covered was discussed as part of the limitations of the study in the revised manuscript (paragraph 3 on page 15).
But I remain somewhat unclear as to how distance from the poverty line was calculated.
Response: The distance was calculated as the monetary value difference between the poverty line and per capita household consumption after paying for cancer treatment. We have clarified the description in the Methods section (paragraph 3 on page 5).
Third, I am unclear as to how national estimates of impoverishment were produced - was the sample weighted somehow?
Response: Thanks for raising this important question. The stratified sampling strategy ensured that the minimal sample size could be met in all of the three regions. However, the eastern region was under-represented. In the revised manuscript, we applied a weighting system based on the number of new cancer cases: 0.48 for eastern, 0.28 for central, and 0.24 for western (paragraph 4 on page 5).
Fourth, access to care will be an important determinant of impoverishment. Care may not have been consumed because it could not be afforded, while this is alluded to it is an issue that is not adequately discussed in the paper
Response: We totally agree. We have added some discussions around this issue. “Accessibility to healthcare services can be seriously jeopodized by low household income especially in a system that requires high proportions of out-of-pocket payments. This study showed an absence of pre-treatment household impoverishment for rural residents. Empirical evidence shows that some households with low income are likely to forfeit expensive medical care including cancer treatment to avoid impoverishment. The actual scale of household impoverishment would be higher should all cancer cases are treated in line with relevant clinical guidelines. Indeed, low household income may

suppress the spending of medical care despite wide coverage of health insurance according to the findings of this study." (paragraph 1 on page 15)
Some more detail on the regression analysis could usefully be provided - I think they used forward selection in choice of independent variables - but they do not discuss goodness of fit.
Response: Thanks for the advice. We have added some details about the regression analyses. The goodness of fit for logistic regression analysis on predictors of the incidence of post-treatment impoverishment in cancer patients has been attached in Table 4.

Reviewer: 3
Reviewer Name: Peter Rohloff
Institution and Country: Wuqu' Kawoq | Maya Health Alliance- Guatemala
Introduction:
- In the introduction or discussion, I think more detail about what the different insurance schemes offer and who they serve would be helpful to help better interpret the results.
Response: Thanks for the advice. We have added some details about the three occupation and employment-based social health insurance schemes (paragraph 9 on page 3).
Also, some discussion of what is publicly paid for in cancer treatment and what patients are typically expected to pay OOP – do we know for example if there are legitimate unpaid costs of treatment or are their illegal or under-the-table user fees?
Response: Thanks. This has been addressed in the methods and discussion sections.
"The entitlements of the three social health insurance schemes varied. However, all had very detailed descriptions of covered items. The insured patients needed to pay for all of the uncovered items (including some drugs for cancer therapy). On top of that, there were deductible (insurance compensations would start only when medical expenditure exceeded a defined minimal level), copayments (share of fee between insurance and the insured), and ceiling requirements (insurance would stop compensations once the expenses reached a defined maximal level)." (paragraph 3 on page 6)
"Previous studies showed that BMIUE had the highest level of compensation rates and the lowest OOP requirements in comparison with the other two schemes. The average payments from the insurance programs for hospital admitted patients were estimated to be around 68% for BMIUE, 48% for BMIUR and 44% for NCMS in 2011. The eastern region offered a higher level of compensations. In Suzhou, for example, 73%, 71% and 56% of hospital charges were covered by BMIUE, BMIUR and NCMS, respectively in 2014. Under-the-table user fees were nominal, if ever existed, due to strict regulations." (paragraph 3 on page 14)
Methods:
- Can you justify the time line (for why the eligibility window was chosen).
Response: The eligibility window was chosen for the purposes of: (1) capturing most expenses related to cancer treatment (two months before and ten months after diagnosis); (2) minimizing recall bias (a full year); (3) meeting sample size requirements (participant recruitments over two years).
- Can you clarify what is meant by exclusion of those with "cancer in multiple organs"? Is this metastatic cancer or two separate primary cancers? If the former, then this is a weakness of the paper and we need some detail about the proportion of cancer that is metastatic and the reasons that it was excluded from analysis. Especially in rural underserved areas I would expect a lot of cancer would be metastatic at diagnosis and represent a very significant portion of the total burden.
Response: Sorry for the lack of clarity. Eligible participants were those who had one primary cancer (including metastatic cancer). Those with two or more primary cancer diagnoses were excluded (paragraph 5 on page 4).
- In the abstract, and methods, the statement about assuming that individuals would divert discretionary spending to cancer treatment, and about treating diagnostic OOP costs as part of pre-treatment consumption – I am unclear on what this means. From reading the methods it seems like OOP costs for cancer treatment were estimated and all household consumption costs were also estimated. I assume the poverty line estimates were based on all household consumption minus

whatever was spent on cancer treatment, so I am unclear what those other statements are meant to indicate
Response: Thanks for the clarification. Yes, this is indeed what we did in estimating post-treatment household consumption. However, for the estimation of pre-treatment household consumptions, we assumed that those households would divert daily consumption money to pay for cancer treatment (paragraph 3 on page 2 & paragraph 4 on page 5).
- Some more detail on how the cost ascertainment tools were developed might be helpful (perhaps an appendix with the tool). Was household income just asked and, if so, how? Or was income estimated from consumption indicators? Are there standard approaches to household consumption measures in the authors' region that were used?
Response: Thanks for the advice. We have added a supplementary file (Table S2) to describe details of household income and consumption items investigated in this study. These items were derived from the National Health Services Survey and the Statistical Bulletin on National Economic and Social Development in China (paragraph 2 on page 6).
Results:
- As the authors note a weakness here is the use of recall data. One possible sensitivity analysis would be to examine for systematic differences in estimates if caregivers vs patients provided these estimates – this would be one way to look at one form of recall variability/bias.
Response: Thanks for the advice. We have performed the sensitivity test by comparing the respondents between patients and caregivers. The results were attached in the supplementary file (Table S1). Overall, the patient estimations were higher those from the caregivers. Such recall bias has been discussed as part of the limitations in the study (paragraph 3 on page 7 & paragraph 3 on page 15).
- Throughout the results section, I wonder about the interaction between the rural/urban and region (eastern/central/western) variable. Particularly that region is significant but urban/rural not in the adjusted regression. I assume region is captured a significant component of "rurality" but can the authors explain this a bit more?
Response: Thanks for raising this important question. We examined the potential interaction between rural/urban and region (eastern/central/western) through: (1) correlation test (weak <0.21); (2) subsample analysis using the urban sample only (regional differences $\chi 2=15.784$, $p<0.001$). Urban-rural differences have limited effects, if any, on the regional differences. (Table S3 & Table S6) (paragraph 1 on page 12)
- -Table 1 could be simplified by eliminating the X2 statistics and leaving the P values and a footnote that these are X2 tests.
Response: Corrected in line with the advice. Thanks.
- For insurance status, does "Others" mean "no insurance" or "private insurance" or both? It seems like this is an important point – explicitly comparing impoverishment by social security vs no insurance status.
Response: The "others" indicate those who were not covered by the social health insurance programs. Private health insurance plays a very limited role, if any, in China. Most private insurance programs are designed as complementary insurance due to almost universal (>96%) coverage of social health insurance. It is unlikely that those who did not enroll in the (cheap) social health insurance programs to purchase (expensive) private health insurance, although we cannot rule out the possibility.
- Seems like a Table that summarizes the key findings of the consumption/income audit would be very helpful. What is the per capita consumption pre and post? How about income? Does income fall post treatment (people losing their jobs)? What are the major categories of consumption and which are most impacted by cancer treatment spending? Where are households deciding to cut costs?
Response: Thanks for the constructive advice. We have added the suggested data in the supplementary file (Table S1). Unfortunately, we were not able to examine whether income fell post treatment (people losing their jobs), which categories of consumption were most impacted by cancer treatment spending, and where households were deciding to cut costs due to limitations of the data

collected. We only collected income and consumption data over a one-year period (two months before and ten months after cancer diagnosis). We acknowledged the need for further studies into these questions.
- Similarly are the details of OOP spending (total amounts and categories) available? Where are the insurance programs failing? What categories of things are people needing to spending money on – for example is it food and lodging or is it payments for stocked out medicines that the public sector should be providing? Where the deficits are says a lot about where improvements could be made or where the problems lie.
Response: Thanks for the suggestion. We provided a supplementary file (Table S1) describing the accumulated consumption gap post cancer treatment in impoverished households in China. However, we were not able to break down these data into the subcategories as suggested. In the discussion section, we have added some details about the role of social health insurance programs. The household impoverishment results can be shaped by many factors. Some households may forfeit needed medical treatments to avoid impoverishment. Others may borrow money to support household consumptions or sacrifice other consumptions to support medical treatments. Further studies are needed to better understand how households cope with the financial burden of cancer treatment. We have discussed the limitations of data collected in this study (paragraph 3 on page 15).

VERSION 2 – REVIEW

REVIEWER	Leng, AnLi Shandong University
REVIEW RETURNED	01-Feb-2021

GENERAL COMMENTS	It's very meaningful study.

REVIEWER	O'Neill, Ciaran Queen's University Belfast Faculty of Medicine Health and Life Sciences, Centre for Public Health
REVIEW RETURNED	16-Feb-2021

GENERAL COMMENTS	The paper has numerous numbering systems in place that should be corrected. The paper acknowledges that impovrishment may e a function of both demand for and cost of services, this should be borne in mind when advocating for policies to address impovrishment. Given access to insurance may be endogenous with income/location some care may be warranted in interpretation of the finding related to insurance status.

REVIEWER	Rohloff, Peter Center for Research in Indigenous Health, Wuqu' Kawoq
REVIEW RETURNED	13-Jan-2021

GENERAL COMMENTS	Authors have comprehensively addressed the reviewer questions.

VERSION 2 – AUTHOR RESPONSE

1.Please further revise your title to make it more neutral. We recommend "Effects of cancer treatment on household impoverishment: a multicenter cross-sectional study in China" or similar.
Response:The title has been revised.
2.Please move the "Patients and public involvement" statement to the end of the Methods section.
Response:The statement of “Patients and public involvement" has been moved to the end of the Methods section.
3.Given access to insurance may be endogenous with income/location some care may be warranted in interpretation of the finding related to insurance status.
Response:This has been revised.
4.The paper acknowledges that impoverishment may be a function of both demand for and cost of services, this should be borne in mind when advocating for policies to address impoverishment.
Response:This has been revised.